



126: 229493f **Synthesis and evaluation of brain-targeted chemical delivery systems for the neurotrophomodulator 4-methylcatechol.** Kourounakis, Angeliki; Bodor, Nicholas; Simpkins, James (Center Drug Discovery, Univ. Florida, Gainesville, FL 32610-0497 USA). *J. Pharm. Pharmacol.* 1997, 49(1), 1-9 (Eng), Royal Pharmaceutical Society of Great Britain. Since various 4-alkylcatechols stimulate nerve growth factor (NGF) biosynthesis both in-vitro and in-vivo, delivery of these agents to the brain may provide beneficial effect for the treatment of neurodegenerative diseases such as Alzheimer's. Several dihydropyridine-pyridinium salt type redox chem. delivery systems (CDS) of 4-methylcatechol (4-methylcatechol) were prepd. as potential brain selective targetry forms for 4-methylcatechol. After preliminary evaluation by in-vitro stability studies in various buffer solns. and biol. media, a selected CDS was further investigated in the rat to det. its in-vivo distribution. Selective and sustained delivery of the compd. of interest to the rat brain was achieved. Furthermore, the NGF stimulatory activity in the rat brain after peripheral administration of the selected CDS was evaluated by measuring the levels of pre-proNGF mRNA in the rat hippocampus and frontal cortex, by dot blot hybridization and anal. Results showed the peripheral administration of the CDS to achieve a 1.7-fold increase in NGF mRNA compared to control in the rat hippocampus, and an approx. 1.4-fold increase in the frontal cortex.

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/30971

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